

## CORRELATION OF SERUM URIC ACID WITH MATERNAL AGE, PARITY AND SEVERITY OF BLOOD PRESSURE IN PRE-ECLAMPTIC PREGNANCIES

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### ABSTRACT

Maternal serum uric acid was determined in 30 pre- eclamptic and 20 normal pregnant females in their third trimester. Serum uric acid was  $3.52 \pm 0.75$  in normal pregnancies and  $6.03 \pm 1.67$  in pre- eclamptic pregnancies. This increase in serum uric acid was highly significant ( $P < 0.001$ ). There was no influence of parity and maternal age on serum uric acid. Serum uric acid levels increased significantly from  $5.05 \pm 0.89$  to  $7.49 \pm 1.50$  with increase in mean arterial pressure above 115 mmHg in pre -eclamptic pregnancies. ( $P < 0.01$ )

**KEYWORDS:** Serum uric acid, Eclampsia, Pre-eclampsia, Hyperuricaemia, Maternal age, Parity, Mean arterial pressure.

### INTRODUCTION

Possible biochemical indices of pre-eclampsia have been sought for many years. Amongst the many markers which have been investigated, perhaps serum uric acid has been considered the most reliable. The relationship between hyperuricaemia and pre-eclampsia was first noted (Slemons and Bogert 1917) and it is now principally agreed that hyperuricaemia is a characteristic of pre-eclampsia (Hill *et al* 1978). Serum uric acid is also a reliable index of foetal welfare when pregnancy is complicated by pre-eclampsia, prognosis of foetus is poor irrespective of level of blood pressure (Verma 1982).

Serum uric acid is one of the parameter used in early diagnosis of pregnancy induced hypertension, and a level of 5.5mg% or more can be taken as a warning sign of pregnancy induced hypertension and is associated with increased perinatal morbidity and mortality (Ranjan *et al* 1996; Lim *et al* 1998).

Various studies have demonstrated a correlation between serum uric acid and pre-edampsia (Voto *et al* 1988; Koike *et al* 1997; Garrone *et al* 1997 and D' Anna *et al* 2000) but information about the influence of maternal age, parity and mean arterial pressure on serum uric acid in pre-eclamptic pregnancies is scanty.

The present study has examined the serum uric acid concentration in pre-eclamptic and normal pregnant females in the third trimester of pregnancy. The influence of maternal age, parity and mean arterial pressure on uric acid is studied.

### MATERIALS AND METHODS

The present study was conducted on proven cases of pre-eclampsia. Thirty pre-eclamptic females in third trimester of pregnancy were selected from Inpatient and Outpatient Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, INDIA, in a period of one year ( March 2002 to February 2003). Exclusion criteria were

associated renal/hepatic/cardiac disorder; metabolic disorders; concomitant severe complications of pregnancy, pregnancy less than 28 wks or more than 41 weeks, multiple pregnancy and any medication during pregnancy except vitamins, iron and calcium (Farah *et al* 1993).

Previously healthy normotensive females were considered to have pre-eclampsia if their blood pressure after 20 weeks of pregnancy was raised to  $\geq 140/90$  mmHg or had mean arterial pressure Continental J. Medical Research 2: 24 - 29, 2008

(Diastolic pressure + 1/3 pulse pressure) of more than 110mmHg. The increase in blood pressure had to be present on at least two occasions 6 hours apart along with proteinuria of more than 300mg/day or 100mg/dl.

Twenty females with normal pregnancies in third trimester were matched on an individual basis for same parameters and were taken as controls.

Table 1. Serum uric acid (mg/100ml) in normal and pre-eclamptic pregnancies:

	Normal pregnancy (n=20)	Pre- eclampsia (n=30)
Uric acid (mg/100ml)	3.52 $\pm$ 0.75	6.03 $\pm$ 1.67*
Age		
<25 yrs	3.48 $\pm$ 0.64	5.58 $\pm$ 1.07
>25 yrs	3.56 $\pm$ 0.81	6.4 $\pm$ 1.97
Parity		
Primipara	3.78 $\pm$ 0.63	5.73 $\pm$ 1.49
Multipara	3.26 $\pm$ 0.8	6.32 $\pm$ 1.85
MAP		
110-115 mmHg	-	5.05 $\pm$ 0.89**
>115 mmHg	-	7.49 $\pm$ 1.5

\* P<0.001

\*\* P<0

All females were between 20-40years of age (mean age 25.53 $\pm$ 3.9 years).

Estimations of serum Uric acid: Phosphotungstate Method (Brown 1945 and Martinek 1970)

Test principle

Uric acid in alkaline medium reduces phosphotungstic acid to “Tungsten Blue” a blue coloured complex which is measured calorimetrically.

Procedure

Preparation of working solution:

0.5 ml of stock uric acid standard was diluted to 50 ml with distilled water and mixed well.

Step A : Deproteinization of sample

1 ml of serum and 8 ml of distilled water was taken in clean, dry test tube to which 0.5 ml sulphuric acid, 2/3 N (Reagent 1) 0.5 ml sodium tungstate and 10% W/N (reagent 2) was added, mixed well and allowed to stand for 10 minutes and then centrifuged.

#### Step B :

Three dry and clean test tubes serving as blank 'B', standard 'S' and test 'T' were taken. 1 ml of sodium carbonate, 14% W/N (Reagent 3) and phosphotungstate (Reagent 4) were added to three test tubes. Then 3 ml of supernatant filtrate (from step A) was added in test 'T' test tube, 3 ml of working reagent was added in standard 'S' test tube and 3 ml distilled water in blank 'B' test tube. Contents of all three test tubes were mixed and allowed to stand in dark for 15 minutes. Optical density (OD) of blank (B), standard (S) and test (T) were measured against distilled water on colorimeter using red filter or at 710 nm wave length.

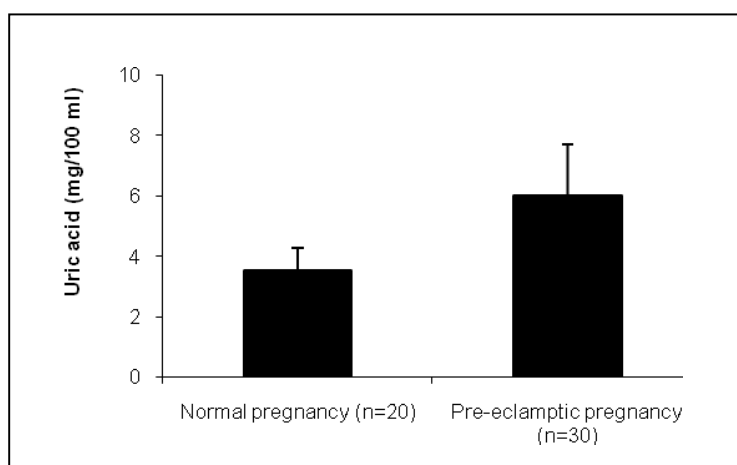


Figure 1 : Serum uric acid in normal and pre-eclamptic pregnancies

#### Calculation

$$\text{Serum uric acid (mg/100ml)} = \frac{\text{O.D test} - \text{O.D. Blank}}{\text{O.D. standard} - \text{O.D. blank}} \times 10$$

#### Statistical Analysis

Values were expressed as mean  $\pm$  SD. Statistical analysis was done using student 't' test. Results were considered significant if 'p' value was  $<0.05$ . Correlation between serum uric acid and mean arterial pressure was determined by co-efficient of correlation (r).

#### RESULTS

The comparison of serum uric acid in normal and pre – eclamptic pregnancies is shown in Table 1 ( Fig – 1). There was a highly significant increase in serum uric acid from  $3.52 \pm 0.75$  in normal to  $6.03 \pm 1.67$  in pre- eclamptic pregnancies ( $p < 0.001$ ).

Serum uric acid in two age group (below 25 years and above 25 years) in normal and pre-eclamptic pregnancies is shown in Table 1. There was no significant changes in two age group ( $P > 0.05$ ) both in normal and pre- eclamptic pregnancies.

Uric acid levels were studied in two parity groups i.e. primiparous and multiparous. No significant change ( $P > 0.05$ ) was seen in two parity groups.

Pre – eclamptic females were divided into two groups according to (MAP) mean arterial pressure (i) MAP 110-115 mmHg (ii) MAP > 115 mmHg. The normal pregnant females had mean arterial pressure below 110 mmHg. Uric acid levels increased significantly from  $5.05 \pm 0.89$  to  $7.49 \pm 1.50$  with increase in mean arterial pressure above 115 mmHg ( $P < 0.01$ ) (Table 1, Fig 2)

Fig 3 is showing the correlation between mean arterial pressure and serum uric acid. There was a direct positive association between serum uric acid and mean arterial pressure ( $r = 0.8$ ,  $P < 0.001$ ) which was highly significant.

## DISCUSSION

The present study demonstrated that serum uric acid levels were significantly elevated in pre-eclamptic pregnant females as compared to normal pregnant females. There was no effect of maternal age and parity in both groups on uric acid levels. But uric acid levels increased significantly in pre-eclampsics with rise in mean arterial pressure more 115 mmHg. Strong positive correlation was seen between serum uric acid and mean arterial pressure.

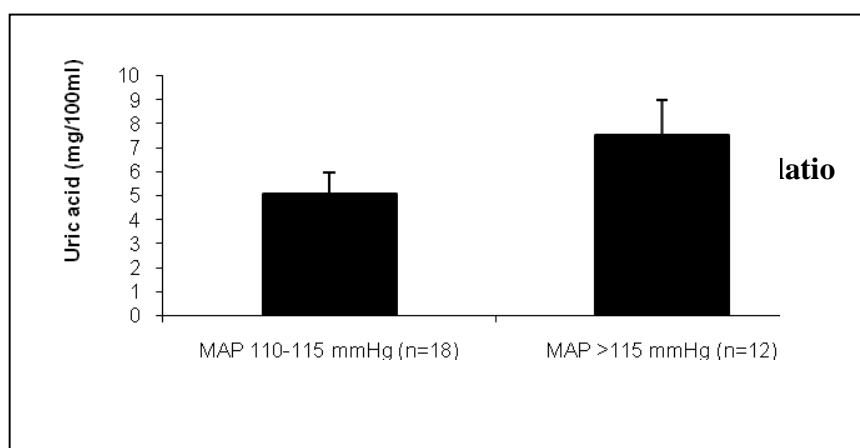


Figure 2: Comparison of serum uric acid in pre-eclamptic women with 2 levels of mean arterial pressure (MAP)

It has been more than 60 years since association between hyperuricaemia and toxemia was first noted<sup>1</sup>. During that time the theories advanced to explain this relationship have included, placental production of uric acid (Fadel *et al* 1969) starvation (Diekmann 1952) lactic acidosis (Handler 1960), excessive muscle exertion (Crowford 1941) hepatic damage (Cadden and Stander 1939) decreased glomerular filtration rate (Schaffer *et al* 1943) and renal cellular damage (Treadwell and Dixon 1961).

In normal pregnancy glomerular filtration rate increases in first trimester and then remains stable until term. The clearance of uric acid, however continues to change as pregnancy advances. Upto 16 weeks of gestation there is decline in serum uric acid concentration and increase in excretion of uric acid. From 16<sup>th</sup> – 36<sup>th</sup> weeks serum uric acid increases whereas excretion remains constant (Hyttén and Lind 1973).

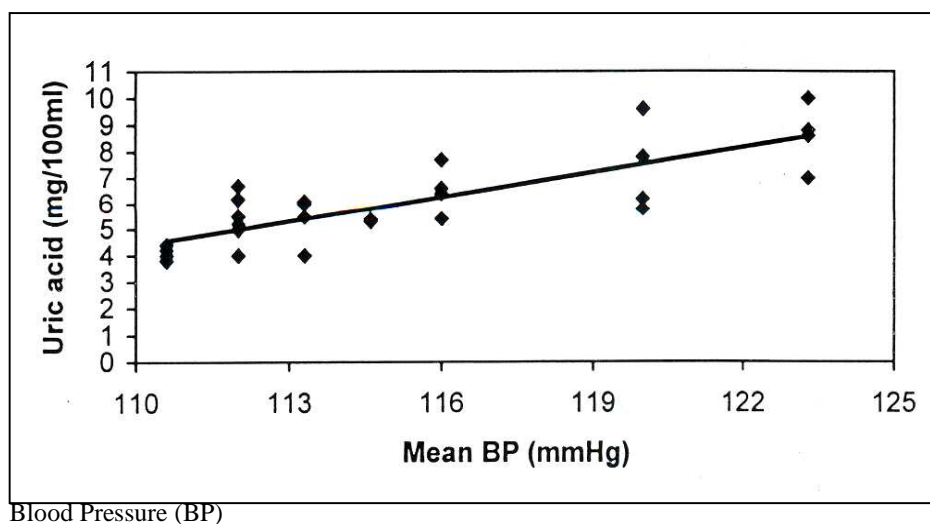
In pregnancy induced hypertension there was impaired glomerular filtration rate and an increased tubular reabsorption of uric acid, leading to impaired uric acid clearance and thereby increasing serum uric acid concentration. Although both glomerular filtration rate and clearance of uric acid were shown to decrease in pre-eclampsia, there was no direct correlation between glomerular filtration and renal handling of uric acid (Chesley and Williams 1945).

Increased oxidative stress and formation of reactive oxygen species had been proposed as another contributing source of hyperuricaemia noted in pre- eclampsia (Many *et al* 1996).

Although hyperuricaemia is an acknowledged characteristic of pre- eclamptic toxemia, (Plass 1924) did not consider the level of uric acid to be an index of severity of disease (Pitchard and Stone 1967) found no evidence to suggest that those with highest serum uric acid were more seriously ill.

According to some worker increased accumulation of lactic acid might lead to decrease excretion of uric acid and thereby resulting hyperuricaemia associated with pre – eclampsia (Stander and Cadden 1934; Quick 1932).

It was demonstrated that a significant but weak correlation between serum uric acid levels and blood pressure (Lim *et al* 1998) but another study showed a highly significant positive correlation as was also shown in this study (Hickman *et al* 1982).



Blood Pressure (BP)

Figure 3 : Correlation of mean arterial pressure with uric acid

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